Perioperative Approach to the High-Risk Cardiac Patient

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Key Points

1. Perioperative triage should determine whether cardiac patients receive outpatient surgery, routine inpatient care, or critical care services.
2. Advanced hemodynamic monitoring may be required in high-risk patients with cardiac disease undergoing noncardiac surgery, including direct arterial pressure measurements, filling pressures, echocardiography, and cardiac outputs.
3. Patients with stable or unstable coronary artery disease (CAD) are commonly seen for noncardiac surgery. The unstable patients present a very high risk and have an increased mortality rate. Perioperative myocardial infarctions are difficult to diagnose and have a poor outcome.
4. The new 2017 guidelines for hypertension have markedly increased the number of patients with this disorder. Many more patients will be seen on antihypertensive therapy when coming for noncardiac surgery. In general, their therapies should be continued throughout surgery, with the possible exception of those drugs that block the renin-angiotensin system.
5. The outcome of patients with heart failure (HF) is worse than that of patients with isolated CAD in the perioperative period. Thus complete evaluation and maximum therapy should be used to reduce morbidity and mortality.
6. Takotsubo cardiomyopathy is a syndrome related to excessive catecholamines and must be differentiated in the surgical patient from acute coronary syndromes or HF. Usually the distinction can be made with echocardiography, and the outcome is often good.
7. The most common types of valvular heart disease seen in noncardiac surgical patients are aortic stenosis and mitral regurgitation. The therapeutic goals and principles used to manage these patients should be similar to those used during cardiac surgery.
8. Atrial fibrillation is the most common arrhythmia seen in older adult patients. Many of these patients are taking anticoagulants to reduce the incidence of stroke. These drugs must be managed well in surgical patients.
9. The new oral anticoagulants consist of a direct thrombin inhibitor, dabigatran, and three factor Xa inhibitors. These drugs have marked advantages over the older warfarin-type anticoagulants. However, experience with them in the perioperative period is still developing, especially regarding the use of regional anesthetic techniques.
Keywords
perioperative triage
coronary artery disease
valvular hypertension
valvular heart disease
arrhythmias
anticoagulants
Approximately 230 million surgical procedures are performed worldwide each year. Perioperative mortality rates are relatively low, but this may be a misleading fact because complications continue to be significant. In fact, high-risk patients may have a postoperative complication rate as high as 50%. This subset of patients accounts for only 13% of all surgical procedures but more than 80% of postoperative deaths. The management of these high-risk patients in the perioperative period presents a unique challenge for perioperative physicians. This chapter focuses on the perioperative management of "high-risk" complex cardiac patients for noncardiac surgery, with additional discussion of common diseases.

PERIOPERATIVE TRIAGE

Defining which patients are appropriate for various perioperative care areas, whether it is outpatient surgery, routine inpatient care, or critical care services, is vital. Triage can be defined as the process of deciding which patients should be treated first based on degree of sickness or severity of injury. In the present value-based health care system, placing the “right” patients in the “right” places is a difficult but crucial task.

Ambulatory Surgery

A challenging triage decision is identifying which surgical patients are best cared for in hospital-based versus ambulatory settings. Adequate preoperative patient assessment is important in determining the appropriate surgical environment. Criteria associated with increased hospital admission after outpatient surgery include age 65 years or older, cardiac diagnoses, peripheral vascular disease, surgery lasting more than 2 hours, cerebrovascular disease, malignancy, HIV diagnosis, and general anesthesia. Data evaluating 5 years of common ambulatory-eligible surgical procedures (≈250,000 procedures) suggest the following risk factors are associated with an increase in morbidity and mortality: previous cardiac surgical intervention (percutaneous coronary intervention [PCI] or cardiac surgery), overweight or obese body mass index, chronic obstructive pulmonary disease, prior transient ischemic attack or stroke, hypertension, and prolonged surgical time (Table 2.1). Patients with stable coronary artery disease (CAD) may not be at higher risk for perioperative complications after ambulatory surgery. Additionally, patients with cardiac pacemakers or implantable cardioverter-defibrillators can be evaluated for ambulatory surgical cases. Important information includes the type and function of these devices before proceeding with surgery. Similarly, it is appropriate to develop a definitive perioperative plan for the management of these devices (in terms of electromagnetic interference and follow-up) (see Chapter 4).

Critical Care Services

Triaging healthy and moribund patients away from critical care services (excluding palliative services and services to those who are brain dead) seems to be relatively straightforward. However, healthcare providers are challenged by a scarcity of intensive care unit (ICU) beds and an inherent cost in determining which patients will truly benefit from intensive care. Improving preoperative evidence-based strategies to identify which patients are at highest risk for postoperative complications may aid in determining patient need. Similarly, reducing hospital variability in managing these patients when they develop postoperative complications is also paramount to
Table 2.1 Factors Associated With Triage Decisions

<table>
<thead>
<tr>
<th>Factors Associated With ICU Admission</th>
<th>Factors Associated With Increased Hospital Admission After Outpatient Surgery</th>
<th>Factor Associated With Increased Risk of Morbidity or Mortality After Day Case–Eligible Procedures</th>
</tr>
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<tbody>
<tr>
<td>Surgical patients (vs. medical patients)</td>
<td>Age &gt;65 y</td>
<td>Previous cardiac surgical intervention (PCI or cardiac surgery)</td>
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<td>Absence of comorbidities</td>
<td>Cardiac diagnoses</td>
<td>Overweight or obese BMI</td>
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<td>Presence of hematologic malignancy</td>
<td>Peripheral vascular disease</td>
<td>COPD</td>
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<td>Acute clinical condition</td>
<td>Malignancy</td>
<td>History of TIA or CVA</td>
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<td>Need for active intensive care therapies</td>
<td>HIV</td>
<td>Hypertension</td>
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<tr>
<td>Trauma</td>
<td>General anesthesia</td>
<td>Prolonged surgical time</td>
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<td>Vascular involvement</td>
<td>Surgery &gt;2 h</td>
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<td>Hepatic involvement</td>
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<tr>
<td>Acute severity of illness</td>
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<td>Lowest surgical Apgar score</td>
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*Depicts the factors associated with ICU admission, increased hospital admission after outpatient surgery, and factors associated with heightened risk for morbidity and mortality after outpatient procedures.

BMI, Body mass index; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ICU, intensive care unit; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

reducing morbidity and mortality. Approximately 30% of patients accepted for ICU services have cardiac diseases.

Observational studies also outline the potential benefit of ICU admission for older adult patients, suggesting a greater mortality reduction in older adult patients admitted to ICUs compared with younger patients. Based on these findings, intensivists may consider accepting even older adults who appear “well.”

Studies evaluating intraoperative events such as blood loss have shown a reduction in mortality rate with ICU admission. Intraoperative hemodynamics and blood loss should indeed influence ICU triage.

**Triaging Patients With Coronary Stents for Noncardiac Surgery**

One of the largest observational studies to date reported an approximately 23% rate of noncardiac surgery 1 year after PCI. Multiple guidelines report that elective surgery should be delayed for at least 4 to 6 weeks after bare-metal stent (BMS) placement and 6 to 12 months after drug-eluting stent (DES) placement, depending on the type of stent. The major challenge is determining the risk of perioperative surgical hemorrhage versus dual antiplatelet therapy (DAPT) interruption, and its relation to subsequent coronary stent thrombosis (see Chapter 3).

A safe time period for antiplatelet therapy interruption has yet to be clearly defined. Still, the continuation of aspirin is often recommended throughout the perioperative
period. In the absence of guidelines supported by strong evidence, it may be important for the care team (primary care doctor, cardiologist, perioperative physicians) to collaborate and develop a definitive perioperative plan regarding continuation of DAPT, type and timing of stent placement, and disposition. Risk factors such as those mentioned may lead the perioperative team to suggest hospital-based surgery with the potential for an overnight stay and monitoring.

s0030 CARDIOVASCULAR SYSTEM

p0100 Cardiac issues remain a significant contributor to perioperative morbidity and mortality. The intraoperative management of cardiac complications in noncardiac surgery is discussed below with a focus on CAD, hypertension, heart failure (HF), valvular heart disease, and rhythm disturbances.

p0105 Patients with underlying cardiac disease may require advanced monitoring throughout the perioperative period. However, there is limited evidence to establish clear guidelines, and clinical discretion is advised. Invasive arterial pressure monitoring may be considered in patients requiring pharmacologic therapy to stabilize blood pressure (BP) or cardiac function. Central venous access may be needed for drug or fluid administration, but central venous pressure monitoring may not reliably reflect intravascular volume status or fluid responsiveness. The role of pulmonary artery catheters in noncardiac surgical and critically ill patients continues to be controversial and depends on local practice patterns. Transeosophageal echocardiography (TEE) or focused transthoracic echocardiography (TTE) may serve as an important monitor in the operating room to evaluate cardiac function and fluid status. An understanding of common cardiac diseases will help perioperative clinicians gauge the level of monitoring and care that is appropriate for each unique scenario.

s0035 Coronary Artery Disease

p0110 Patients with or at risk for CAD present significant challenges to anesthesiologists in the perioperative period. As many as 5% of patients with CAD undergoing noncardiac surgery may develop cardiac complications. Risk factors include a history of ischemic heart disease, HF, stroke, diabetes mellitus, or renal insufficiency. Preoperative risk stratification is discussed in detail in Chapter 1. Perioperative acute coronary events may range from myocardial ischemia or myocardial injury to myocardial infarction (MI). MI is universally defined as an elevation of cardiac biomarkers such as troponin, electrocardiographic (ECG) changes, new regional wall motion abnormalities seen on echocardiography, or coronary catheterization findings consistent with acute blockages.

p0115 The perioperative management of acute coronary syndrome (ACS), unstable angina, or acute MI presents a unique challenge because these patients under anesthesia or sedated postoperatively may not have the same signs and symptoms often seen in nonoperative patients. In fact, one large study found that 65% of patients with perioperative MI did not have symptoms. Thus the diagnosis is often confirmed only when clinical suspicion leads to further laboratory testing or investigation. When patients do complain of symptoms or clinical suspicion exists, clinicians should obtain a 12-lead ECG and serial cardiac biomarkers (e.g., troponin). Cardiology consultation for risk stratification, further testing, and therapy may be warranted.

p0120 Unlike nonsurgical patients with ACS or MI, care pathways for perioperative patients are not well studied. Unique concerns such as bleeding risk, surgical stressors, and perioperative physiologic changes make protocols for therapy very challenging.
Management must be considered in context for each patient and the relative risk-to-benefit ratio of therapies applied uniquely.

Patients with ACS preoperatively must first be clinically stabilized. Therapies to augment cardiac output may be needed. Administration of β-adrenergic agonists (e.g., dobutamine [2.5–5 µg/kg per minute] or epinephrine [1–2 µg/min]) can be effective. Mechanical augmentation with devices such as an intraaortic balloon pump or axial-flow pumps may be considered in severe cases. Arrhythmias may occur and should be managed, but prophylactic lidocaine is not indicated.

Medical therapy with aspirin (162–325 mg) should be initiated if not contraindicated. Additional antiplatelet therapy with a P2Y₁₂ receptor blocker is indicated in ACS, but may not be safe in the perioperative period. In patients with non–ST segment elevation ACS or MI (non-STEMI), systemic anticoagulation (i.e., heparin infusion) may be indicated, but the risk of surgical bleeding must be weighed against the risk of advancing ACS. Oxygen should be administered to all hypoxic patients in concentrations needed to achieve normoxia. There are no data to support the use of oxygen in patients with MIs and normal oxygen saturation. Nitroglycerin may be administered to patients with angina, but should be avoided in patients with severe aortic stenosis (AS), right ventricular infarction, hypotension, or a history of phosphodiesterase inhibitor use in the previous 24 hours. Caution should also be used with this vasodilator in patients under neuraxial anesthesia because this could precipitate hypotension. Pain control with opioid analgesics may be considered; however, evidence suggests that morphine may be detrimental in patients with ACS. Proposed mechanisms include a morphine-induced impaired absorption or effectiveness of certain antiplatelet therapies. Statin therapy is indicated as soon as possible (Box 2.1).

β-Blocker therapy is perhaps the most controversial perioperative cardiac therapy. Although several studies have shown improved cardiac morbidity and mortality with the administration of perioperative β-blockers, concern for increased stroke risk and all-cause mortality has been noted. Current guidelines recommend that patients on chronic β-blocker therapy continue this perioperatively. In the setting of perioperative ACS, β-blocker therapy may decrease demand ischemia by improving oxygen supply and demand imbalance and is indicated in stable patients with ACS. The use of β-blockers in unstable patients or patients with acute cocaine intoxication should be cautioned.

Angiotensin-converting enzyme (ACE) inhibitor therapy should be considered in ACS after patients are stabilized. Angiotensin receptor blockers (ARBs) may be substituted in patients with HF with a left ventricular ejection fraction (LVEF) less than 40% or significant kidney dysfunction (creatinine >2.5 mg/dL for men or >2.0 mg/dL for women).

**BOX 2.1 Management of Acute Myocardial Infarction/Acute Coronary Syndrome**

- Oxygen to maintain normoxia
- Aspirin 162–325 mg
- P2Y₁₂ antiplatelet therapy
- Systemic anticoagulation (if no contraindication)
- Nitroglycerin for pain (if no contraindication)
- Opioid analgesics as needed
- β-Blockers if stable
- Statin therapy as soon as possible

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The optimum hemoglobin level in patients with perioperative ACS or MI is not known. Routine red blood cell transfusion in stable, nonbleeding patients may not be indicated when the hemoglobin is above 8 g/dL.

More aggressive interventional therapy with cardiac catheterization or fibrinolytics is dependent on the type of myocardial injury and risk of surgical bleeding. STEMI presents a high mortality rate if left untreated. In the nonsurgical setting, patient outcome is clearly related to time to reperfusion with a recommended "door to reperfusion time" of less than 90 minutes. The mainstays of reperfusion therapy include (1) cardiac catheterization and angioplasty or stent placement or (2) fibrinolytic therapy. Multiple studies have shown an improved survival rate, fewer bleeding complications, and reduced recurrent MI with catheterization and PCI. These interventions present significant concerns in the perioperative period because of an increased risk of bleeding.

Fibrinolytic therapy is often reserved for centers without PCI capabilities. It is recommended when symptom onset is less than 12 hours before presentation and PCI would not be available within 120 minutes. However, in the perioperative setting, fibrinolytics are almost universally contraindicated because of bleeding risk. PCI may be better suited for the treatment of perioperative STEMI. This is not without risk, however, because angioplasty or stent placement often requires DAPT and anticoagulation. Finally, emergent coronary artery bypass graft (CABG) surgery is an option, although this is associated with increased mortality rate when performed in the first 7 days after STEMI. Close consultation with cardiology and surgery is needed to weigh the risks and benefits of therapeutic options in perioperative STEMI patients.

Patients with NSTEMI may be managed more conservatively. However, in patients with a low cardiac output syndrome or arrhythmias, emergent PCI and reperfusion may be warranted. In stable NSTEMI patients, noninvasive studies may be the first approach. Again, close consultation with cardiology will aid in risk stratification and management.

Patients with significant chronic stable CAD also can present for noncardiac surgery. These patients may have either severe multivessel disease or left main CAD. Both portend an increased risk in the perioperative period. Significant left main disease or its equivalent is an indication for CABG. Occasionally, however, emergency noncardiac surgery may be needed before definitive CAD treatment. The risks and benefits of noncardiac surgery in these patients should be considered carefully in consultation with a cardiologist or cardiac surgeon.

Anesthetic management in these patients should be geared toward preventing, monitoring, and detecting myocardial ischemia. Careful monitoring of the ECG and hemodynamic status is important. Hemodynamic goals include a low-normal heart rate, normal to high BP, and normothermia. Left ventricular distention caused by fluid overload should be avoided because increased wall tension may increase myocardial oxygen demand and decrease myocardial perfusion. Additional monitoring may be considered, including perioperative TEE. Medications with more favorable hemodynamic profiles (e.g., etomidate) should be considered for anesthetic induction and maintenance. Pharmacologic therapy in the form of inotropic support may be needed. Mechanical support of the heart with an aortic balloon pump or axial flow devices may help maintain coronary perfusion in the setting of severe disease. Additional anesthetic considerations must be based on patient- and procedure-specific needs.

Hypertension

Hypertension is a common perioperative illness that has included roughly one third of all noncardiac surgery patients in the past. The new 2017 guidelines on hypertension...
define a normal BP as less than 120/80 mm Hg. Elevated BP is systolic BP between 120 and 129 mm Hg and diastolic BP less than 80 mm Hg. Stage I hypertension is now a systolic BP between 130 and 139 or diastolic BP between 80 and 89 mm Hg. Stage II hypertension is systolic BP greater than 140 and diastolic BP greater than 90 mm Hg. These new guidelines state that BP should be treated earlier to avoid complications, and with these new definitions, nearly half of the U.S. population will be considered to be hypertensive. Chronic hypertension is associated with an increased risk of stroke, heart disease, and renal failure.

Patients presenting on the day of surgery with high BP represent a clinical challenge. Safe systolic BP cutoffs for elective surgery are not well established. Uncontrolled hypertension is listed as a "minor" risk factor by the American College of Cardiology/American Heart Association (ACC/AHA), and it remains unclear if postponing surgery for uncontrolled hypertension improves patient outcome. Diastolic BP is better studied, with the preponderance of evidence suggesting safely proceeding with elective surgery if the diastolic BP is below 110 mm Hg. The relative risks and benefits of surgery in the setting of hypertension should be considered by the care team on a patient-by-patient basis.

Most preoperative antihypertensive medication can be continued in the perioperative period. Renin–angiotensin system blockers are associated with intraoperative hypotension and vasoplegia. Therefore many centers hold ACE inhibitors or ARBs for 24 hours before surgery, although this practice is controversial. A decrease in intraoperative hypotension is noted when these medications are held. On the other hand, failure to restart ACE inhibitor or ARBs has been associated with an increased 30-day mortality rate. The initiation of new medications immediately before surgery, such as β-blockade, may increase the risk of stroke or death. These medications should not be started preoperatively unless there is sufficient time for the patient to acclimate to the new medication before surgery. Patients taking β-blocker or sympatholytic agents should continue these medications perioperatively because acute withdrawal symptoms can occur if these agents are stopped.

Appropriate BP monitoring must be considered on a case-by-case basis with patient and surgical considerations in mind. Patients with chronic hypertension are at increased risk for hemodynamic lability. Anesthetic goals, therefore, include maintenance of hemodynamic stability within a range of BP. A reasonable goal is to maintain the BP within 20% of a patient’s baseline. In addition, blunting of the sympathetic response to anesthetic (laryngoscopy) and surgical stimuli should be attempted with anesthetic agents or adjunct medications. Relative hypotension can be treated with vasopressors with the goal of maintaining BP within a predefined range.

Severe hypertension must be managed expeditiously if end-organ complications are to be avoided (i.e., neurologic, cardiac, renal). First-line therapy with intravenous antihypertensive medications (e.g., calcium channel blocker, nitrates, β-blockers) is recommended. Postoperative complications related to elevated BP, such as surgical bleeding, must also be considered when determining the level of urgency in BP therapy.

Hypotension unresponsive to standard therapy may require further investigation. Surgical bleeding or manipulation of the vasculature may induce low BP and communication with the surgical team is vital. Myocardial ischemia or arrhythmias should be considered. Less common, but an important consideration, is the vasoplegic syndrome (VS), which is defined as severe hypotension refractory to catecholamine therapy without clear cause. The incidence of VS is highest in cardiac surgical patients, but it may be seen in noncardiac surgery as well. Exogenous vasopressor (dose of 1–2 units) may improve hypotension when conventional therapy has failed (i.e., decreasing anesthetic agent, volume expansion, and routine vasopressors). Alternatively, methylene blue (MB) is a well-described treatment. It is believed to
interfere with the nitric oxide–cyclic guanylate monophosphate pathway, decreasing its vasorelaxant effect on smooth muscle. A bolus dose of 1 to 2 mg/kg over 10 to 20 minutes followed by an infusion of 0.25 mg/kg per hour for 48 to 72 hours is typical. Recently, the use of hydroxocobalamin (vitamin B12; dose of 125–250 mg) has been recommended in the occasional complex patient who does not respond to the above treatments.

**Heart Failure**

Heart failure represents a significant perioperative complication presenting in up to 10% of patients after major noncardiac surgery. A preoperative history of HF may increase cardiac risk substantially, especially in the presence of risk factors such as CAD and diabetes. HF is broadly defined as a syndrome of impaired cardiac function and is often categorized into systolic failure associated with reduced ejection fraction (HFrEF) and diastolic failure with preserved ejection fraction (HFpEF).

Similar to perioperative ACS, care pathways for the perioperative management of patients with HF are ill defined and poorly studied. Retrospective cohort studies using data from large national databases have helped elucidate risk factors, but it remains unclear how specific therapies may affect outcomes in the perioperative period. Patients may present with dyspnea, orthopnea, tachypnea, or clinical signs such as crackles or decreased oxygen saturation. Signs of right-sided HF may also be present, including nausea and vomiting, lower extremity edema, and hepatic congestion. This may present a confusing clinical picture because many of the signs and symptoms of HF may be seen in the perioperative period because of other causes such as surgical insult, pain, and medication side effects.

Clinical suspicion of HF should prompt further investigation that includes an ECG, chest radiography, and cardiac biomarkers. Elevated brain natriuretic peptide (BNP) is supportive of the diagnosis of HF. Some patients with chronic HF may have a baseline abnormal level of BNP, and further elevation of BNP from baseline may be diagnostic of an acute exacerbation. Initial laboratory evaluation also should include electrolytes, renal and liver function tests, hemoglobin, and echocardiography.

Therapies may be tailored to specific causes. Treatment must be directed at managing concomitant respiratory failure; adequate oxygenation and ventilation are paramount to normalizing cardiac function. Electrolyte imbalances and acid–base disturbances should be corrected to minimize potential detrimental effects on ventricular contractility, pulmonary arterial pressure, and cardiac rhythm. Preload, contractility, and afterload must also be optimized.

In patients with signs of volume overload, diuretic therapy and fluid restriction are mainstays of therapy. Patients with HFrEF with clinical signs and symptoms of low cardiac output may benefit from inotropic therapy (e.g., dobutamine). In the setting of failed pharmacotherapy, mechanical devices may be used to treat severe HF (e.g., intraaortic balloon pump, ventricular assist devices).

In patients with stable hemodynamics, ACE inhibitor and β-blocker therapy is recommended by the ACC/AHA. Additionally, in patients with reduced ejection fractions, newer therapies such as combinations of valsartan and sacubitril (Entresto) are recommended to improve outcome. Readers are referred to the clinical guidelines from the ACC/AHA for more detailed information.

**Takotsubo Cardiomyopathy**

Approximately 2% to 3% of patients presenting with ACS meet diagnostic criteria for takotsubo cardiomyopathy (TCM). It is important to distinguish patients with
Perioperative Medicine

TCM from those with ACS or HF because the etiology and treatment of each differ substantially.

Current data point towards a high level of circulating catecholamines as the predominant factor leading to TCM. Mammalian hearts have been found to have higher levels of β-adrenergic receptors in the apical ventricular myocardium. This phenomenon is believed to mediate an increased sensitivity to catecholamine surges in the apex of the heart. Clinically, the resultant myocardial dysfunction occurs disproportionately in the apex of the left ventricle, resulting in pathognomonic apical ballooning seen on echocardiography or ventriculography. Estrogen helps regulate the sympathetic response to catecholamines, blunting this response in reproductive years. This may explain why a predominance of TCM is seen in postmenopausal women.

Clinically, TCM often presents with a preceding physical or positive or negative emotional stressor (“happy heart syndrome” or “broken heart syndrome”). Certain diseases have been associated with TCM, including sepsis, pheochromocytoma, cerebral hemorrhage, respiratory failure, and thyrotoxicosis. Acutely, a hypertensive response to catecholamines may be noted followed by cardiomyopathy, hypotension, and HF.

Differentiating TCM from ACS is crucial. ECG findings play an important role, and abnormal findings are typically present. ST-segment elevation in lead aVR is found to have a high positive predictive value for TCM. In contrast, ST-segment depression in leads V₃ to V₄ makes ACS more likely. Non–ST segment elevation TCM is commonly associated with T-wave inversions in leads I, aVL, V₅, and V₆. However, NSTEMI is associated with ST-segment depression in V₂ and V₃ (anterior wall MI). Laboratory findings classically depict a mild elevation in cardiac biomarkers with TCM. The degree of wall motion abnormality is often disproportionately large compared with the degree of biomarker elevation in TCM. Echocardiogram findings often reveal circumferential wall motion abnormalities with the classic finding of apical ballooning occurring in 80% of cases. Other variants such as basal (see later) and midventricular types have been described. Regional wall motion abnormalities outside of a single coronary artery’s distribution can help distinguish TCM from acute MI. In addition, coronary angiography typically reveals nonobstructive or absent disease (Box 2.2).

The treatment of patients with TCM may vary depending on the clinical scenario. Serious cardiac complications can occur in up to 20% of patients with TCM. Apical hypokinesis coupled with a hyperkinetic basal region can lead to left ventricular outflow obstruction. This should be managed with the cessation of inotropes and fluid administration to decrease turbulent flow through the outflow tract. Delaying elective surgery should be considered in the setting of TCM. In cases in which surgery is deemed necessary, care must be taken given possible cardiogenic shock,

**Box 2.2 Diagnostic Features of Takotsubo Cardiomyopathy**

- Precedent physical or emotional stressor
- Signs or symptoms of heart failure
- Mild elevation in cardiac biomarkers with disproportionately large wall motion abnormality seen on echocardiography; classically, apical ballooning
- Ventricular involvement extending beyond one vascular territory
- Normal or nonobstructed coronary arteries on angiogram

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HF, or hemodynamic instability. Invasive monitoring with an arterial catheter, TEE, or both should be considered. Inotropic support should be used judiciously because catecholamines are associated with precipitating TCM. Mechanical support may be considered in low-output states. In patients with HF, standard therapies previously described are applicable, including diuretics and fluid restriction. Recovery usually occurs over days to weeks. Longer term, therapeutic blockade of the renin–angiotensin system and adrenergic system may be useful in preventing recurrences of TCM and reducing the longer term structural, functional, and metabolic changes that may follow episodes of TCM.

Reverse takotsubo syndrome (rTTS) is a more recently described variant of TCM characterized by basal hypokinesis and apical hyperkinesis. Diagnostic criteria remain similar to TCM, with hallmark echocardiographic findings of wall motion abnormalities in the basal region extending beyond a single coronary vascular territory. Similar to TCM, rTTS is thought to be caused by a relative increase in catecholamines and subsequent myocardial toxicity. Patients with rTTS often present at a younger age than those with TCM. This is thought to be due to an age-related increase in apical adrenergic receptors compared with a more basilar distribution in young people. rTTS has a lower risk of cardiogenic shock than TCM but may have higher biomarkers than the more common apical variant. This is thought to be due to a larger area of myocardial involvement. Treatment is mainly supportive, and the long-term prognosis is good.

Valvular Heart Disease

Concomitant valvular heart disease may be common in the perioperative period. Depending on the severity of valvular disease, surgery and anesthesia may present a significant physiologic challenge. An understanding of the type and severity of valvular disease can help the clinician tailor care appropriately. Preoperative echocardiographic evaluation may help guide perioperative management. A clinical suspicion of undiagnosed valvular disease or recent changes in clinical history should prompt preoperative echocardiographic testing if none has been performed in the previous 12 months. A broad overview is discussed below, but a much greater degree of detail can be found in Kaplan’s Cardiac Anesthesia, 7th edition.

Aortic Stenosis

Aortic stenosis is the most common form of valvular heart disease and a major predictor of morbidity in noncardiac surgery. In patients 75 years of age or older, AS is a common finding, with an incidence of 3% to 8%. Decreased cardiac reserve blunts the ability to respond to the physiologic stressors of surgery and anesthesia, likely accounting for an increased perioperative morbidity and mortality. In addition, AS may be associated with an increased risk of bleeding caused by an acquired form of von Willebrand disease. Perioperative management of patients with AS may require invasive hemodynamic monitoring, especially in major noncardiac surgery, to assure proper loading conditions and avoid potentially catastrophic decreases in preload and afterload that may lead to ischemia, left ventricular failure, and cardiac arrest.

Therapeutic goals are similar both intraoperatively and postoperatively. Hypovolemia and tachycardia should be avoided because the left ventricle is often hypertrophied and noncompliant and thus more dependent on adequate filling time and elevated filling pressures to maintain preload. Sinus rhythm should be maintained because left ventricular filling is also increasingly dependent on atrial contraction in the setting of AS. Systemic vascular resistance (SVR) should be maintained, and significant decreases in BP should be avoided because they may cause dangerous reductions in
coronary perfusion (Table 2.2). Neuraxial anesthesia may cause a decrease in SVR and preload and should be considered with great caution in patients with AS. Phenylephrine or norepinephrine are effective medications for maintaining SVR in the perioperative period.

### Aortic Regurgitation

The risk of noncardiac surgery in patients with aortic regurgitation (AR) relates directly to the severity of valvular disease, the cause of AR, and the surgical risk. Moderate to severe AR and intermediate- to high-risk surgery are risk factors for increased pulmonary edema, prolonged intubation, and in-hospital death.

Understanding the degree of AR preoperatively is key when caring for these patients. In patients with severe AR and poor LVEF (<50%), valve repair or replacement may be considered before elective noncardiac surgery.

Many anesthetic agents cause a decrease in SVR, reducing regurgitant fraction and improving AR. Nevertheless, careful management is necessary. To maintain forward cardiac output, avoidance of bradycardia is important because it may increase regurgitation due to increased diastolic time. Similarly, hypertension and volume overload should be avoided. The use of diuretics and afterload reduction medications may be helpful.

### Mitral Stenosis

Patients with moderate to severe mitral stenosis (MS) undergoing noncardiac surgery present a significant challenge to clinicians. LV filling is impaired because of obstructed flow across the stenotic mitral valve. Supraventricular arrhythmias may develop because of structural changes in the left atrium (LA). Pulmonary hypertension can develop because high LA pressures are transmitted backward to the pulmonary vasculature. Eventually, patients with severe MS can develop pulmonary edema and right ventricular (RV) failure.

Caring for patients with MS in the perioperative period involves maintaining LV filling pressures and optimizing conditions for right heart function. Care must be taken to avoid hypercarbia, hypoxemia, and acidosis, all of which can increase pulmonary vascular resistance and impair RV function. Inotropic support of the RV may be needed. Dobutamine is a reasonable choice, with phosphodiesterase inhibitors such as milrinone reserved for more critical scenarios.

Medications that cause tachycardia such as ketamine and anticholinergics are best avoided. A slow heart rate allows for improved LV filling across the stenotic mitral valve; β-blockers such as esmolol should be available. Anxiolysis to avoid tachycardia is important, but care must be taken to avoid hypercarbia or hypoxemia with sedation. Avoidance of hypotension may be achieved with “hemodynamically stable medications” such as etomidate. Regional and neuraxial anesthesia may be used, but clinicians should attempt to avoid hypotension. Epidural anesthesia with gradual dosing of medication may reduce the risk of sudden hypotension.
Mitral Regurgitation

Patients with moderate to severe mitral regurgitation (MR) undergoing surgery are at increased risk of perioperative morbidity and mortality. Those with chronic MR have long-standing volume overload of the LV, which leads to dilation of the ventricle and left atrium. Because of compensatory mechanisms, chronic MR is often well tolerated by patients. Acute MR, however, is not well tolerated and is often complicated by overt HF, pulmonary hypertension, and pulmonary edema. The most common cause of acute MR is ischemia causing papillary muscle dysfunction. Addressing the underlying cause of acute MR is the mainstay of management.

Key management principles for patients with chronic MR undergoing noncardiac surgery include maintaining sinus rhythm and avoiding bradycardia, hypertension, and volume overload. Sinus rhythm is crucial because atrial contraction may account for 30% to 40% of LV end-diastolic volume. Atrial fibrillation (AF) significantly decreases LV filling and can lead to HF and shock. Most anesthetic agents improve MR by decreasing afterload and thus decreasing LV systolic pressure. Regional or neuraxial anesthesia may be reasonable in the absence of contraindications for placement such as chronic anticoagulation for AF. Diuretics and afterload reduction should be considered if volume overload or hypertension is encountered.

Arrhythmias

Atrial Fibrillation

Atrial fibrillation can be defined as the lack of coordinated contraction of the atria. The ECG reveals an irregular R-R interval and absent P waves. Perioperatively, a multitude of factors can precipitate AF, including direct surgical irritation of the atria or pulmonary veins, fluid shifts and electrolyte imbalance, or catecholamine surges related to pain or the stress of surgery. AF is associated with an increased risk of stroke because slow blood flow through the atria can lead to thrombus formation, particularly in the left atrial appendage.

In patients with AF, the decision of when to stop oral anticoagulants preoperatively is a source of continued concern. Patients at particular risk of stroke may be “bridged” from the time of cessation of oral anticoagulants to surgery with low-molecular-weight heparin (LMWH) or unfractionated heparin. The duration of cessation and timing of bridging therapy are decided on an individual basis based on surgical risk of bleeding and patient risk of thromboembolism. The management of anticoagulation therapy should be coordinated with the managing physician (e.g., primary care doctor or cardiologist).

The new non–vitamin K oral anticoagulants (NOACs; see the NOAC section for more detail) such as the direct thrombin inhibitors (DTIs) and factor Xa inhibitors pose a significant concern in surgical patients. There is far less experience regarding the safe timing of cessation; 3 days is usually adequate with normal renal and hepatic function. Furthermore, reversal with antidotes has recently become available, but there is little clinical experience with these drugs. The American Society of Regional Anesthesia has published guidelines on the timing of regional or neuraxial anesthesia in the setting of oral anticoagulants.

Perioperatively, the hemodynamic consequences of AF are of particular concern, especially in the setting of preexisting cardiac conditions. The loss of atrial contraction coupled with beat-to-beat changes in ventricular filling can lead to suboptimal ventricular preload and decreases in cardiac output and BP. Irregular electrical transmission through the atrioventricular (AV) node can lead to a rapid ventricular response.
Patients with AF in the operative or critical care setting should initially be evaluated for signs of hemodynamic compromise and categorized as stable or unstable. Unstable patients should undergo immediate cardioversion. It should be recognized that cardioversion might increase the risk of stroke, especially in patients with a history of AF and not on anticoagulation. If possible, evaluation for existing intracardiac thrombus with TEE should be considered. In stable patients, rate control with medications and anticoagulation are the mainstays of therapy.

Several different classes of medication can be used for rate control. The most common medications are calcium channel blockers, β-blockers, amiodarone, and digoxin. Therapy must be individualized to the patient and clinical scenario.

**Supraventricular Tachyarrhythmia**

The term supraventricular tachyarrhythmia (SVT) refers to any arrhythmia originating above the AV node. It can be subdivided into irregular and regular rhythms. Regular SVT includes AV nodal reentry, AV tachycardia in both orthodromic and antidromic forms, AV junctional tachycardia, and other less common types.

In the perioperative period, several pathophysiologic mechanisms may precipitate SVT. Common causes include acidosis, hypercarbia, hypoxemia, electrolyte disturbances, hypotension, mechanical irritation of the atria or pulmonary veins, medications, and myocardial ischemia. Investigation into the precipitating factor is a key component in the management of SVT and includes laboratory analysis and ECG.

Treatment is determined by the stability of the patient. Unstable patients require synchronized cardioversion and should be managed with Advanced Cardiac Life Support (ACLS) guidelines in mind. In stable patients, vagal maneuvers (e.g., Valsalva maneuver) may be attempted first. Although carotid massage is a known vagal stimulant, caution should be used because inadvertent carotid injury and stroke have been described. Adenosine temporarily slows conduction through the sinoatrial node and renders the AV node refractory to depolarization. This transient effect makes adenosine a reasonable choice for the treatment of patients with narrow-complex SVT. In the absence of underlying structural heart disease (e.g., AS, MS), SVT is often stable, and rate control with β-blockade, calcium channel blockers, or amiodarone is reasonable.

The treatment of wide-complex SVT and reentrant tachycardia may be more complex. Disorders with accessory pathways, such as Wolff-Parkinson-White syndrome, may respond paradoxically when conduction through the AV node is slowed. Amiodarone may be considered in these situations along with cardiology consultation.

**Ventricular Arrhythmias**

Ventricular arrhythmias arise below the AV node and are typically a wide-complex rhythm. These most commonly originate in scarred or damaged ventricular muscle, creating a conduction pathway outside the normal His-Purkinje system. Wide-complex ventricular rhythms should be differentiated from SVT with abberancy because the treatment may differ.

Ventricular tachycardia (VT) can be subdivided into nonsustained (NSVT) and sustained VT. NSVT is defined as three or more premature ventricular contractions with a rate of 120 beats/min or more, lasting less than 30 seconds. In the absence of underlying disease (e.g., MI), aggressive therapy is likely not indicated. In patients with myocardial injury and poor ventricular function, more aggressive therapy may be indicated, and consultation with cardiology is recommended.

Sustained VT can be subdivided based on morphology into monomorphic and polymorphic types. Monomorphic VT demonstrates a consistent QRS amplitude and is often related to a reentrant pathway within scarred myocardium. Urgent synchronized cardioversion (50–100 J, biphasic) is often required. As with other arrhythmias, treatment
of the underlying cause should be established. Continued therapy with amiodarone or lidocaine by infusion may be indicated in the perioperative period. Polymorphic VT may be associated with normal or long QT intervals, and causes may vary. Normal QT polymorphic VT is often associated with myocardial ischemia. Prolonged QT forms may be related to medications such as sotalol (torsades de pointes), precipitated by underlying genetic predisposition (long QT syndrome), or both. Treatment includes correction of underlying electrolyte disturbances, intravenous magnesium (2–4 g), and asynchronous cardioversion. Consultation with cardiology is likely warranted.

Brugada syndrome is an autosomal dominant hereditary disease characterized by ST-segment elevation in the right precordial leads on the ECG, which predisposes to sudden cardiac death caused by polymorphic VT or ventricular fibrillation in the absence of structural heart disease. The disease affects young and active individuals with a life expectancy of more than 30 years. Life-threatening ventricular arrhythmias occur without obvious causes in about 20% of patients. Multiple therapies have been tried with variable success. The present therapy is to insert automatic internal defibrillators in these patients. However, if a surgical patient does not have one, an external defibrillator with pads should be in place for noncardiac surgery.

PERIOPERATIVE MANAGEMENT OF ANTICOAGULATION

The perioperative management of patients taking anticoagulants for venous thromboembolism (VTE) or pulmonary embolism prophylaxis, AF and stroke avoidance, artificial mechanical valves, or other indications can be challenging. Balancing the disease risk with the risk of surgical bleeding presents an ongoing clinical challenge. Strategies are discussed in the next sections. Risk factors for bleeding in chronically anticoagulated patients include mechanical mitral valve prosthesis (requires higher level of anticoagulation), cancer, history of bleeding complications from anticoagulation, restarting heparin anticoagulation within 24 hours of surgery, and heparin bridging. The decision to stop, continue, or bridge anticoagulant therapy must be considered in the context of patient- and procedure-related risk factors, such as a high risk of stroke from AF or low surgical bleeding risk (e.g., cataract surgery). This section provides a brief review of the anticoagulants, the suggested timing of cessation before elective surgery, and anticoagulation reversal agents for emergent surgery or bleeding complications. Alterations in these medications are best coordinated with the managing physician.

Warfarin (Coumadin) impairs the coagulation cascade by interrupting the carboxylation of factors II, VII, IX, and X, as well as the synthesis of proteins C and S. The resultant anticoagulated state can be monitored with the prothrombin time (PT) or international normalized ratio (INR). Cessation of warfarin 5 days before surgery is a recognized strategy. Postoperatively, warfarin can be reinitiated when the risk of thromboembolic disease outweighs the risk of bleeding. Patients may require bridging therapy with LMWH. The continuation of warfarin throughout the perioperative procedure may be acceptable in certain situations (e.g., cataract surgery), and warfarin may be beneficial in some procedures such as catheter ablation of AF in which the perioperative stroke risk is high and surgical bleeding risk is low. Several modalities of warfarin reversal exist, including vitamin K, fresh-frozen plasma, and prothrombin complex concentrates (PCCs). Activated factor VII may be
considered as well. Reversal agents should be chosen based on the relative level of urgency, pharmacologic properties, and their associated side effect profiles.

**New Oral Anticoagulants**

New pharmacologic agents have been developed with more specific inhibition of the coagulation cascade than warfarin. Several potential advantages over warfarin have been described: no requirement for serial laboratory testing, decreased dietary restrictions, and few drug interactions. These include DTIs (e.g., dabigatran) and direct factor Xa inhibitors (e.g., rivaroxaban, apixaban, and edoxaban). Notably, these medications have been shown to have a decreased risk of intracranial hemorrhage versus warfarin. Until recently, the newest factor Xa inhibitors have had a decisive disadvantage to warfarin in the perioperative period since no specific antidotes existed, and the treatment of serious and life-threatening bleeding could be difficult. Four-factor PCCs are nonspecific but potentially useful reversal agents for the NOACs when hemorrhagic complications occur. In 2018, the Food and Drug Administration approvedandexanet alfa as a reversal agent for the factor Xa inhibitors.

**Direct Thrombin Inhibitors**

There are several DTIs, including hirudin, argatroban, and bivalirudin. The most commonly used intravenous agent is argatroban, which is often used in patients who develop heparin-induced thrombocytopenia. Argatroban undergoes hepatic metabolism, and its elimination is independent of the kidneys, making it ideal for critically ill patients at risk for kidney injury. The anticoagulation effect can be measured by the partial thromboplastin time (PTT) with a goal 1.5 to 3 times the patient’s baseline. Argatroban infusions should be stopped 2 to 4 hours before an intervention or surgery. Confirmation of normal coagulation can be made by a normalization of the PTT.

Dabigatran (Pradaxa) is an oral, reversible DTI that is indicated for treatment of AF and VTE prophylaxis or treatment. Dabigatran use with artificial mechanical valves is unproven and not indicated at present. Caution should be used in patients with renal impairment because the half-life of dabigatran may be increased from 12 to 24 hours. Routine coagulation tests such as the PT and PTT may be altered with dabigatran; however, the degree of alteration and the presence of a normal test result do not exclude impaired coagulation. A normal dilute thrombin time suggests that the anticoagulation activity of dabigatran has resolved; this is the most specific and clinically useful measurement of this drug’s activity. The AHA/ACC suggests that dabigatran should be held for at least 2 days before surgery and a dilute thrombin time obtained to confirm normalization. It is recommended that patients with renal dysfunction should have surgery delayed at least 5 days. The timing of neuraxial anesthesia in patients who have stopped dabigatran is not well defined. Dabigatran should be restarted after surgery when the risk of thrombosis outweighs the risk of bleeding because the onset of anticoagulation is very rapid.

In the past, treatment of serious and life-threatening bleeding was difficult with dabigatran because there was no specific antidote. Key steps included cessation of the drug and supportive care. In life-threatening bleeding, dialysis could facilitate faster removal of dabigatran from plasma. Four-factor PCCs and activated factor VII were considered in life-threatening bleeding from dabigatran, but these were of unproven efficacy. Consultation with a hematologist was warranted.

In 2016, the Food and Drug Administration approved use of idarucizumab (Praxbind) to reverse dabigatran in patients with severe bleeding or requiring an urgent procedure or surgery. This drug is a monoclonal antibody fragment developed...
specifically to reverse the anticoagulation produced by dabigatran. In a study of 500 patients (RE-VERSE AD study) with a prolonged dilute thrombin time, a single dose of 5 g was adequate in 98% of patients and lasted for 24 hours. No other therapy was needed in the surgical patients.

**Factor Xa Inhibitors**

p0520 Factor X is produced in the liver by a vitamin K–dependent process, and the activated form converts prothrombin to thrombin. Oral inhibitors of activated factor X, rivaroxaban (Xarelto), apixaban (Eliquis), and edoxaban (Savaysa), have been shown to be effective in the prevention of stroke in patients with nonvalvular AF. In addition, there is a decreased rate of major bleeding when compared with warfarin. Factor Xa inhibitors are indicated for VTE treatment and prophylaxis, including in postsurgical patients after major joint arthroplasty. Factor Xa inhibitors are associated with a decreased incidence of bleeding versus LMWH. Similar to dabigatran, they are not indicated for treatment of artificial heart valves. Specific laboratory assays of factor Xa inhibitors are available; however, routine monitoring of anticoagulation is not required. The safety of these three drugs with neuraxial anesthesia does not have a large database, but the American Society for Regional Anesthesia says that it can be used after 3 days of drug withdrawal. Bridging for procedures is not necessary for oral factor Xa inhibitors because they have short half-lives. Discontinuation of these factor Xa inhibitors for 3 days is considered appropriate for most elective surgical procedures.

p0525 A specific reversal agent for oral factor Xa inhibitors has recently been approved in the United States. Andexanet alfa has been designed specifically to reverse factor Xa inhibitors. It is a recombinant, modified human factor Xa decoy protein that binds to factor Xa inhibitors. The administration of an andexanet alfa bolus and 2-hour infusion results in rapid and substantial reversal of anti–factor Xa activity for 12 hours.

**SUGGESTED READING**


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